The Genomic Structure of the Mouse Csx/Nkx2-5

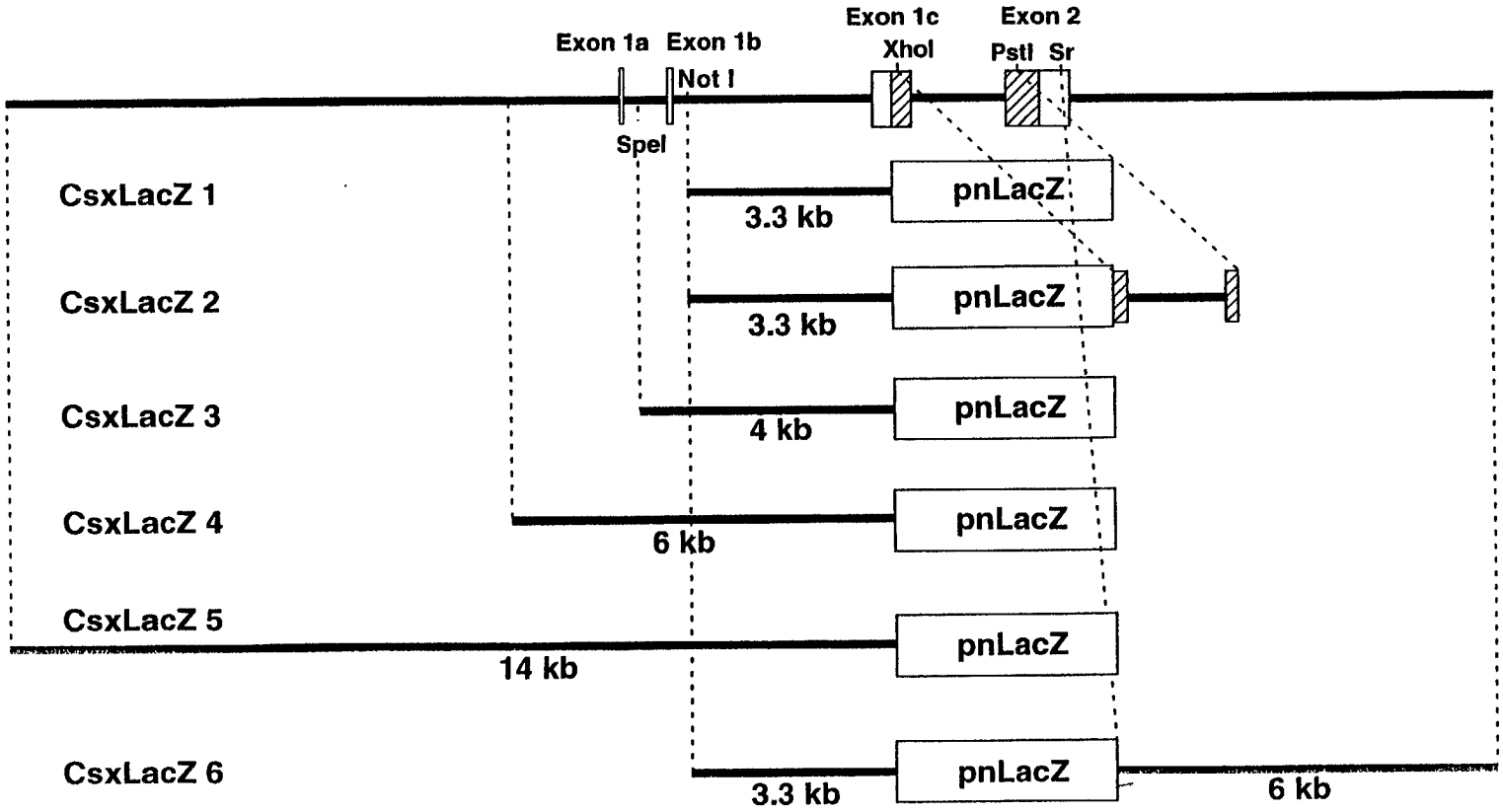


Fig. 1

The Locations of the Csx/Nkx2-5 Cardiac Enhancers

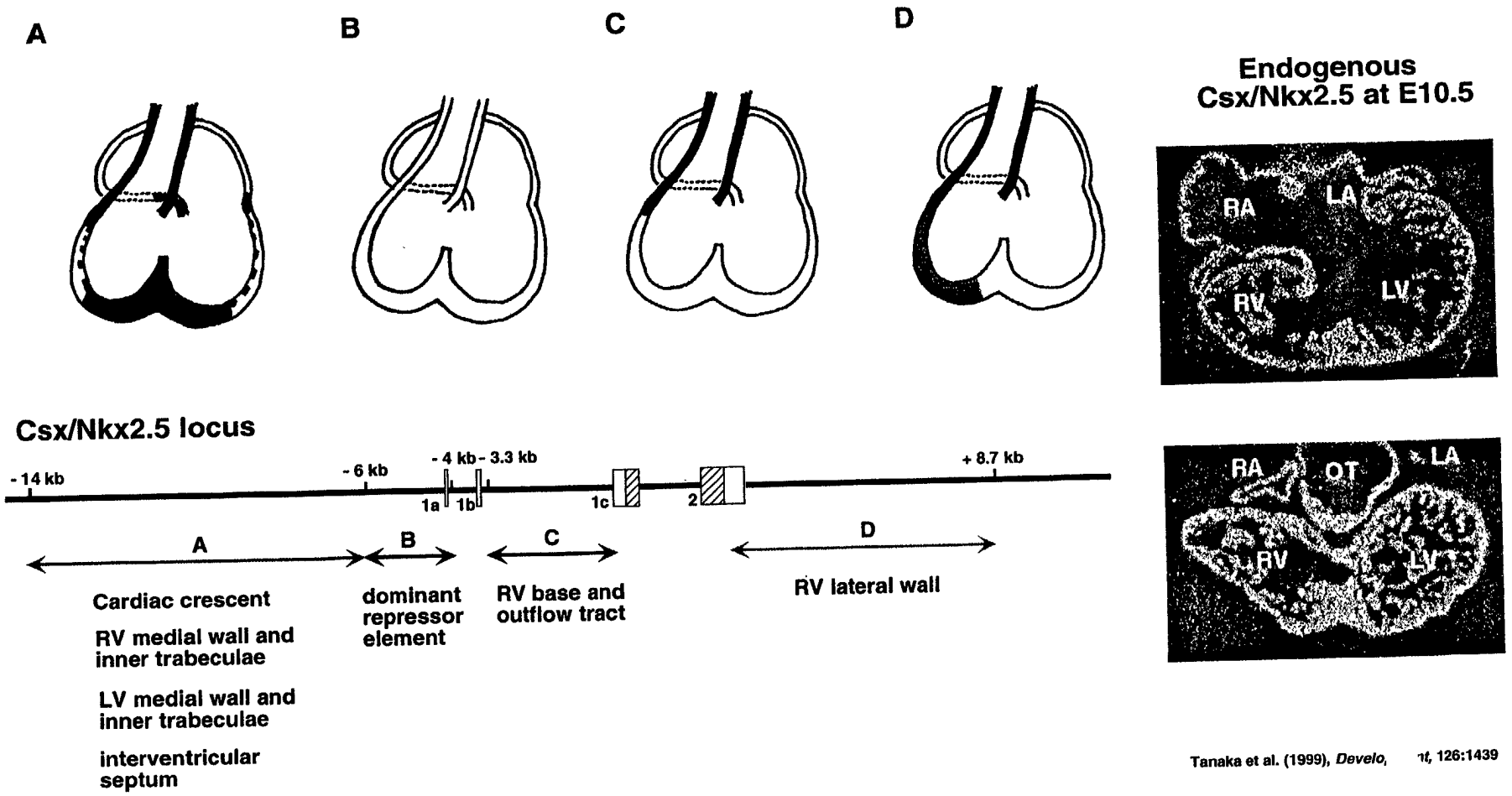
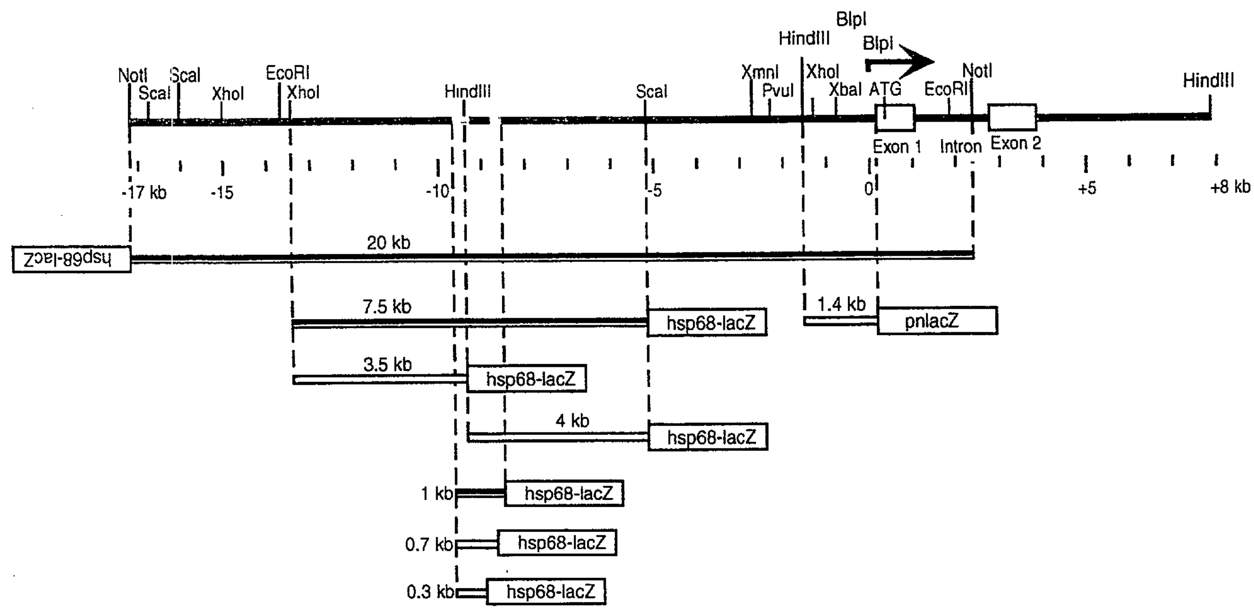


Fig. 2

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             *   * * **   *    *     **  *   **   *    * ** *     * *    *    *   ** **      **  **  * **** *   *    **
                                                     <Sp-1                                     Sp-1>
Human   101 ACCAGCCTCGGGTTCTAGGCCCCCCGCACCCTCATCCTGGCTCCCGCCCCTTCTCTCCACCCTCCCGGACCCCTAAAGGGGCGGCGGGGCCCAAGCGGAG  200
Mouse    96 -CCAGTGACCCGCTCCATGTCCCA-GAATCTTCATGCGGGCTGCAGCATCTCCTTCCCACCCTCCAGGAACGC--GAAGGACAGCGG------AGCCGAG  185
             ****   *  * ** * * ***  * * * **** * **** * **  ** **  ********* *** * *   * ** * ****       *******

Human   201 GGCGCTGCGCCTGACCCCGAGCGGAAGGGCCCCAGTCTAGGTCCTAATGCGGGTGGCGTCTCCTTTGACAGGCGGCGTTTGGGGACAACAGCGGGGACGA  300
Mouse   186 GGGGCAGCGCGTGACCCCGAGCGGAAGGGCGCCAGTCTGGGTCCTAATGCGGGTGGCGTCTCTCTTGACAGGCAGCGTTTGGGGACAACAGCGGGGAAGG  285
            ** ** **** ***************************** ************************* ********* ************************* *
              GATA>            <dHAND   TGF-b>                                           <MEF2
Human   301 GAGATAAGGTGACATACCAGAGCAGATTTGGTGCGGCGCTGATACTCCTCTCCCGACAGGAAACGCGGAGCTATTTAAAA-GACCCTATCGATTACTTT  399
Mouse   286 GAGATAAGATGACATACCAGAGCAGATTTGGTGTGCGCGCTGATACTCCTGGCCCGACAGGAAACTCGGAGCTATTTAAAAAGGCCCTATCGATTACTTT  385
            ******** ************************ **************** ************ *************** * ****************
            <GATA
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Mouse   386 ATCTTCCCCGGAGGAAATCTTGCCGAGAGACAAAAGATGTCCCCCTACCTAAAGATACAAGGCCACACAGCAGAGGGTTTGTACAGGCGACGCGCGAGTA  485
            ***** ** ***       ****** **************** *** * ******** ************* * ****** ** *********** * * *
                                                                                                  Sp-1>
Human   499 GGCGCGGGGAAAGCAAAAACACACTGACGCTTAGAGTGCACAAACGTGTGTGTTCCCAGAGCAGCTCCAGAGTGCGGCAGGGACGCTGGGGGCGGCGAGG  598
Mouse   486 GATCCCTGGGAGCGCAGAGACGCCTTTCTACCGGCAGAGACTGAAGTTTGACTGGAGCGAGGCGGGGCGGAGCCACCTCCCGGTCCCCGTGCACTCCGGA  585
            *   * ** *   * *   ** *   *    ** * ** ** *   *** *  * ***                *   *   *   * *
                                                                                                     <Csx
Human   599 GGCACCCACAGTATGGTCTTCTGTGCCCTTGGAAAGTTTTTTTCACCGTATGCGCGTAAAACACGCACACACAGAGAAAGTGACTGTGCACTTAGGGCG  698
Mouse   586 ATTGTGAACGCTCCCGCAAAGTCCCCGCGAGTGTTGTGTTCACACTAATTGGTGTGCCTCTGAGTTCC------------------------------  653
                  *  *   *    *  * *  *  ** **   *   *            *

Human   699 CCTGTGTGTACCCGTGTCGTTTTAGCGAATTTAAAGCACATCAGGCCGGGCGCCATGGCTCACGCCTGTAATCCCAGCACTTTAGGAGGCCGAGGCGGGC  798
Mouse       ----------------------------------------------------------------------------------------------------

Human   799 CGATCACCTGAGGTCGGGAGTTCGACACCAGCCTGGCCAACATGGTGAAACCCTGTCTCTACAAAAAATACAAAAATTAGCCGGGCATGGTGATGCGTGC  898
Mouse       ----------------------------------------------------------------------------------------------------

Human   899 CTGTGATCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCGGAGGTTGCAGTGAGCCGAGATCACACCACTGCACTCCAGCCT  998
Mouse       ----------------------------------------------------------------------------------------------------

Human   999 GGGCGACAAGAGCGAAATTCCGTCTAAAAAAATAAAATAAAATAAAATGATAATTAAGCCCATCAACTCACATTCAAAGCGGTTACTGGTGGTTGTAATG 1098
Mouse       ----------------------------------------------------------------------------------------------------
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Mouse   654 ----------ATCCGTACTCCCCCCCCCCAAGTTTAAATGCTCCTTTTAAGGGCTTGAGTGTCTGCAGCCGTCATGTGCACCTTGAAAGCTTGGCGTGT  743
                       * *  **       *            ******************** ******** * ******** ** ** ****  ***  ***

Human  1199 GTCAACACGACCCTTTCTAGCGCGCTCGTTTCGTGTCTGAATCCCCGCATTTCGCCAATTTGCTTGGAGCGCAGAACGCCCTCCGCGAAAGGCGGCTGCT 1298
Mouse   744 GACATTGTGTTCCTCTAGCGTCTCCATCCCGCTTTTCACCAATTCGTGCCCTGGCCGAATCCCGTGGAGCAGAGGTGGCCCCTCGAAGTCCCGGGCCAC  843
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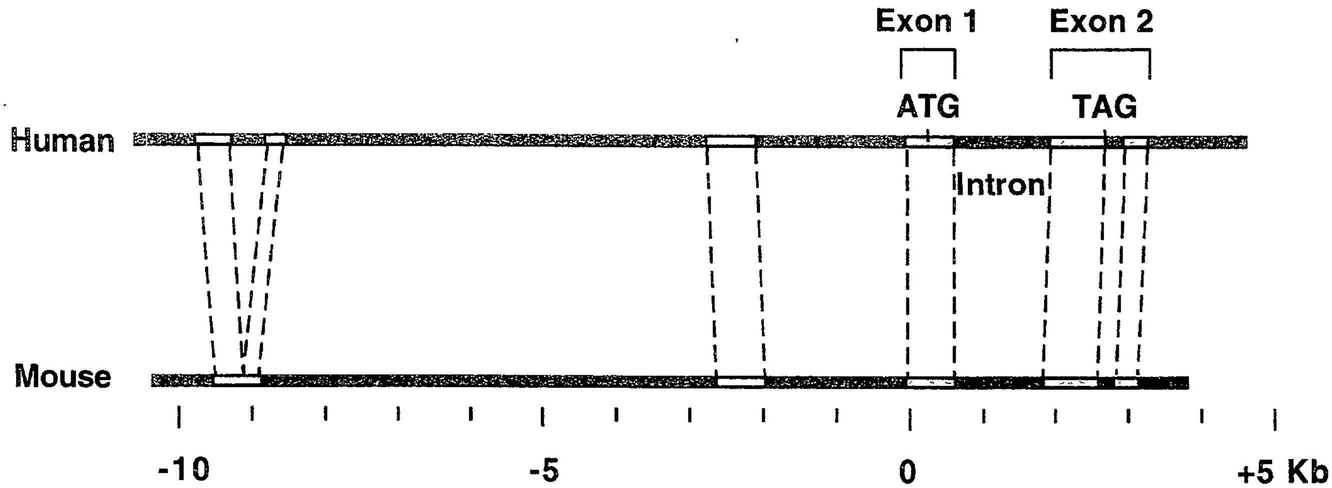
Fig. 3A

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Mouse    1  GAAGAGAAAGGCCAGGGCCTT-TTCACCAAGGTTGTAG-GGGTGGGAAAGTCACTGATTTTGTTCAAATTAGAAGAGTTTT-----CTTCCTTTTTCTTG  93

Human   97  ACACCTGACCCACAGGACTGACAGTTCTAGGAAGCCCCCTTACCCGAAAATAGGAAATAAATCCTTGCCACCTTGATTTGCAAGGGCAATGCTAATTTTT 196
Mouse   94  ACACCTGACCCACAGATTTGTCAACTCT-GGAAGCCCTTATATCCGAAAA-AAGTGATAAATCCTCACCACATTGATTTGCAAAGGAAACG--------- 182

Human  197  TTCTTTCTCCAGAGCTCTCAAAAAAAAAAAAAAAAAAAACCTTACTAAAAACAGGGATCCCGGATGTAGCCTCGATGTCCCCCATTAAACGGTAATATTTC 296
Mouse  183  -TCCCCTCTCAAAACTATTTTTAAAAAAGACTTAAAACAGGGATCCCGGATGGGGGCCCCAATATTGCTCC------CCCAATTAAACGGTAATATTTC 275

Human  297  AGGCGTCCGCTCACACTAATCTTTCAAACTGTCATCGCGAGCCGCCTGGCCAGCAGATTCACTT-AACAGCGCTCCCAGGACCCTCGTTCCGAGCTCTTT 395
Mouse  276  AGGCGTCAGCTCACACTAATCTTTCAAACTGTCATCGCGATCCGCAGGGGCAGCCGATTCACTTTAACAGGACTCCCAGGACC-TCGCCCGAAGCTGTTT 374

Human  396  TCAGCGAGACATTTAATTGAATCGGATGTGGCTCGTTTGCCAGACGTCACCGCCTCGGCGATAGGCATCCTCTCCAACGACACCCCCCCCGCCCGCGCT 495
Mouse  375  TCAGCAAGACATTTAATTGAATCGGATGTGGCTCGTTTGCCAGACGTCACCGCCTGGGTGATAGACATCCGTCCAACCCACACAAACCAATCTTCAATCT 474

Human  496  CGAAAACAATCTTCA  510
Mouse  475  CGGGAGGGTCCCAAGC 490
```

```
Human    1  TAGGAAAAAAAAAAAAAAAGGAAGCCCTCCGGGAGAGACATGCGCCCTAATATTTCTCCCAGATGGGCCGGGTTCAAGCGCGTTTGAGAGTTTGCTCTCCT  100
Mouse    1  CACACAGACAAGCAGTCAATGCGCTGTTTGGCTGTTCCTTGTGTT----TGTGGTTGAAAAGCGGTCCACACACACCCGT-TCTGAGTGACAGTGTGCC-   95

Human  101  ACCAGCCTCGGGTTCTAGGCCCCCCGCACCCTCATCCTGGCTCCCGCCCCTTCTCTCCACCCTCCCGGACCCCTAAAGGGGCGGCGGGGCCCAAGCCGAG  200
Mouse   96  -CCAGTGACCCGCTCCATGTCCCA-GAATCTTCATGCGGGCTGCAGCATCTCCTTCCCACCCTCCAGGAACGC--GAAGGACAGCGG------AGCCGAG  185

Human  201  GGCGCTGCGCCTGACCCCGAGCGGAAGGGCCCCAGTCTAGGTCCTAATGCGGGTGGCGTCTCCTTTGACAGGCGGCGTTTGGGGACAACAGCGGGGACGA  300
Mouse  186  GGGGCAGCGCGTGACCCCGAGCGGAAGGGCCCCAGTCTGGGTCCTAATGCGGGTGGCGTCTCTCTTGACAGGCAGCGTTTGGGGACAACAGCGGGGAAGG  285

             GATA>                  <dHAND   TGF-b>                                                   <MEF2
Human  301  GAGATAAGGTGACATACCAGAGCAGATTTGGTGCGCGCGCTGATACTCCTCTCCCGACAGGAAACGCGGAGCTATTTAAAA-GACCCTATCGATTACTTT  399
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           <GATA
Human  400  ATCTTTCCTGGAAAGCTTCTTGCGGAGAGACAAAAGATGTTCCC-TGCCTAAAGACACAAGGCCACACAACGGAGGGTCTGCACAGGCGACGCACAATTC  498
Mouse  386  ATCTTCCCCGGAGGAAATCTTGCCGAGAGACAAAAGATGTCCCCCTACCTAAAGATACAAGGCCACACAGCAGAGGGTTTGTACAGGCGACGGGCGAGTA  485

Human  499  GGCGCGGGGAAAGCAAAAACACACTGACGCTTAGAGTGCACAAACGTGTGTGTTCCCAGAGCAGCTCCAGAGTGCGGCAGGGACGCTGGGGGCGGCGAGG  598
Mouse  486  GATCCCTGGGAGCGCAGAGACGCCTTTCTACCGGCAGAGACTGAAGTTTGACTGGAGCGAGGCGGGGCGGAGCCACCTCCCGGTCCCCGTGCACTCCGGA  585

Human  599  GGCACCCACAGTATGGTCTTCTGTGCCCTTGGAAAGTTTTTTTTCACCGTATGCGCGTAAAACACGCACACACAGAGAAAGTGACTGTGCACTTAGGGCG  698
Mouse  586  ATTGTGAACGCTCCCGCAAAGTCCCCGCGAGTGTTGTGTTCACACTAATTGGTGTGCCTCTGAGTTCC--------------------------------  653

..uman 699  CCTGTGTGTACCCGTGTCGTTTTAGCGAATTTAAAGCACATCAGGCCGGGCGCCATGGCTCACGCCTGTAATCCCAGCACTTTAGGAGGCCGAGGCGGGC  798
Mouse       ----------------------------------------------------------------------------------------------------

Human  799  CGATCACCTGAGGTCGGGAGTTCGACACCAGCCTGGCCAACATGGTGAAACCCTGTCTCTACAAAAAATACAAAAATTAGCCGGGCATGGTGATGCGTGC  898
Mouse       ----------------------------------------------------------------------------------------------------

Human  899  CTGTGATCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCGGAGGTTGCAGTGAGCCGAGATCACACCACTGCACTCCAGCCT  998
Mouse       ----------------------------------------------------------------------------------------------------

Human  999  GGGCGACAAGAGCGAAATTCCGTCTAAAAAAATAAAATAAAATAAAATGATAATTAAGCCCATCAACTCACATTCAAAGCGGTTACTGGTGGTTGTAATG 1098
Mouse       ----------------------------------------------------------------------------------------------------
```

Fig. 3B

The Genomic DNA Sequence Homology Between Human and Mouse Csx/Nkx2-5

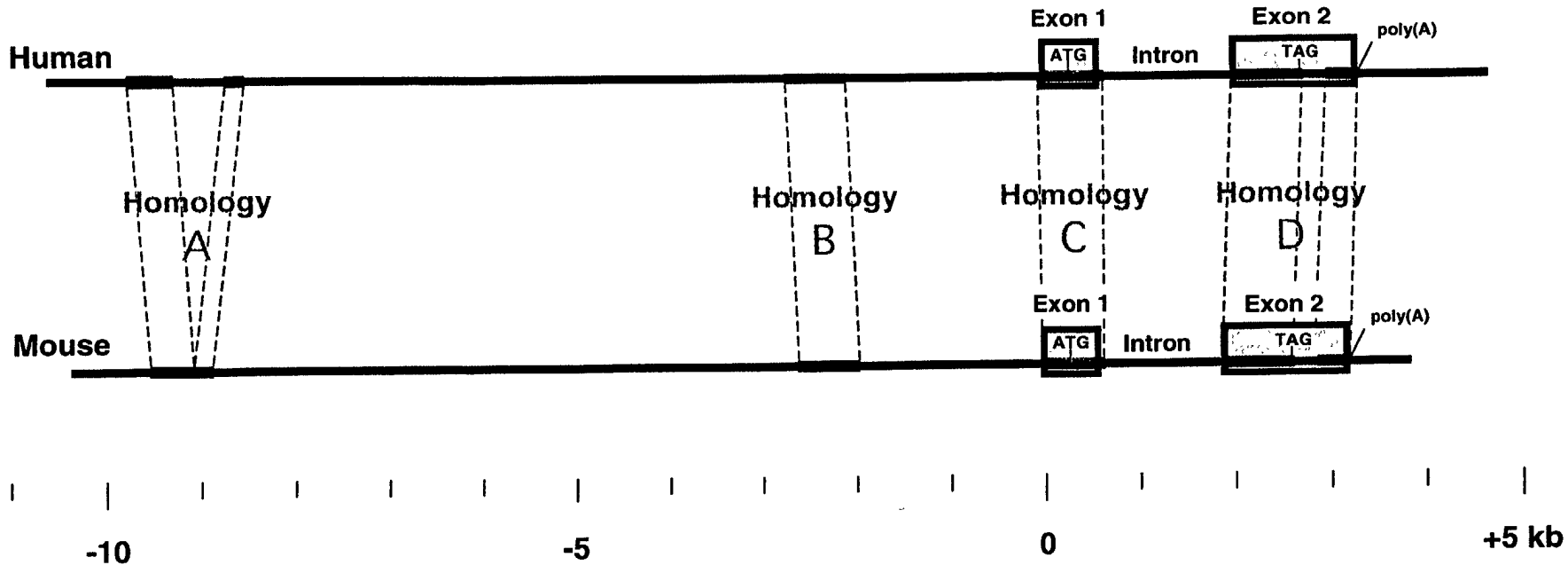

Fig. 3C

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Fig. 4A 1

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Fig. 4A 2

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Fig. 4A 3

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Fig. 4A 4

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AGGGCGTTGCGCGCCTCCTGGGCTGCCCTGCGGGGCTCACCTCTCTCCCCAGCATGGAGG
CCCCAGGTCCTGGGAGTGTGGCTTTGATGAGGGACAGGAAAAGTCCCAACATCAGGCCAA
TGCTTGACTTCACTTGCGTCGGCGTCTCAGACGGCACACTGTCGGGTTTGAGCACCCAAG
ATGTACGTTCTGGACAGACACTATTTTGTCCCCATACATGGAGCGTTTCCTCCGCACCTT
GGGCGCGCCTGCGGGAGCTGTGTCTTTAGGTAGTTTTTGGCCCTGCGCCGCCTTTATTCT
ACTCCAAGCGCTCTTTGCCAAACCCGCACTCCGCAAAGAGCCAAGCCCTCCACATCCCCA
TTCTCAGCAAGTCCACGCGTCCCGCCCAGCTTCCCGCCCGCGGTTCCCTGTACCAGCTAG
GGCCGTGAGAAGCCAACGCTTTTCCACTGACAAATCCTGTCATCCCCAGCTCTAGAAGGC
GTCCTTAACCTGGGCCCGCTCTGCCTGCCCGGACTCCTGAATTGTAAGCAAAATAAAACT
CCTCTCTGCAGTGTTCTGGGGAATGGAGAAGACCCCAAGCTTTCATCAGACCCTCCCAAG
GAGTGCGGGGACCCAGAGAAATGAGGCCACCCGGGCAGGATCTGGCCATGTAGCTGGCGC
TCCTGAAACTCTGGCAGATTTGTCTGACTTCTGTGCCCTACTCTACTGACCCTGGGCTAA
AAATGATCATGATCACCCCACTTGCCCTGCCCTTCCCCCACGCGCCTGACCGAGCCGCAG
GGGTGCCCCACTGGAAGTCCGGCCCAGAGGCCTCAGAGAAATCCTGGCCTAGCTGGGCTC
AGAGGAGCCCCGCCTCCCTGAGAGCTAAACCTGGGCTAGGACCCTGAAACCTCGAGGTTG
GCAGAAGCCTGAGGGCCTTGCTGCCAGGCAGGGAGGGCACGGGAAGGAGGGAGGTGGGAT
CGATGGCCTCCAAACAGGGGAAACAAGGTGGCTGGTAGCTGGGGCACTCCACAAGACAGG
TGTNTCCTGGGAAGCTGAGCTTACCAGCTGGGATTCCTGATTTATTTCATTATTAAGGGG
AGAGGCATTTCCCCTGGGAGGGTACTGGCAGTGACTGATGCCCCCTGGAGTTGTGCTGTG
CATAACACTACTGTAGGAGGCAGCAACTCCTACCCCACCTGGCCATCACTCACCTTGCCC
TTACTTTCGTTGATTCGCCCAGAAGCACCCAGAGCCTGCGGCATGATTGACCCTGTAGGC
CAAGCCAAACCAAACCCCCGAATTGTCCAGAATTTTCGCCCTGGTGTATCCCCAAAGCCC
AGCCCTGTCTTTNAGGGTTTTTTTCCTATTGAGATTTTCCCTCATCCCACCACCTTTAGT
AATAAAGCCTTCCTCAAACTAATTTCCTCCCCACCGCTTCCCACCCCATCCTTTTTTTTT
CCCATGCTGGTTTGGGTGCTGAGGAATATTTTTTCAAACCCACACCCATCCAGCCCTGCC
CAGAGGCCTGACTTTGCATGCCTCTGGTAGGNTTTTCAGGGTTACATTAGGGAGCAAAAG
CAGGGTGCAGGGGCAAAAGGGGACCCTTCCAAATGGGTCGTGGCCCCTTTAAAAAAGCTG
GGCAGGGNTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGCCGTATGACTATA

Fig. 4B 1

TTAGGTGACACGAAACTGCTCATCGCTCCTGTCATCGAGGCCCCTGGCCCAATGGCAGGC
TGAGTCCCCCTCCTCTGGCCTGGTCCCGCCTCTCCTGCCCCTTGTGCTCAGCGCTACCTG
CTGCCCGGACACATCCAGAGCTGGCCGACGGGTGCGCGGGCGGGCGGCGGCACCATGCAG
GGAAGCTGCCAGGGGCCGTGGGCAGCGCCGCTTTCTGCCGCCCACCTGGCGCTGTGAGAC
TGGCGCTGCCACCATGTTCCCCAGCCCTGCTCTCACGCCCACGCCCTTCTCAGTCAAAGA
CATCCTAAACCTGGAACAGCAGCAGCGCAGCCTGGCTGCCGCCGGAGAGCTCTCTGCCCG
CCTGGAGGCGACCCTGGCGCCCTCCTCCTGCATGCTGGCCGCCTTCAAGCCAGAGGCCTA
CGCTGGGCCCGAGGCGGCTGCGCCGGGCCTCCCAGAGCTGCGCGCAGAGCTGGGCCGCGC
GCCTTCACCGGCCAAGTGTGCGTCTGCCTTTCCCGCCGCCCCCGCCTTCTATCCACGTGC
CTACAGCGACCCCGACCCAGCCAAGGACCCTAGAGCCGAAAAGAAAGGTGAGGAGGAAAC
ACAGGCCCCCTTCTCCCCTCCTGGGTCGCTTTCGTCCCCAAGAAACTCAGGGCCAGGAGG
AGGACACACGCGCCCTTGGGCCGAGGGCTGGGCTGCGGCGGGGGGTTCAGAATGTAAGAT
GCCTGGTGTTGTCGCCAGGCTCCCGCGCCCCGCGTCCAATCGGAGGTTCAGAGGAAATGC
CGGATTGAAAGGATCCGAAAGCAAGAGACCAAAAAACTTTTCCCCCCGGCCTAACAAACC
CCCGGCGGTTTCCGCTCTGCTCCTGGTTCTGGTAGAATTTTAAAAATCGGTTTATGGTTA
AACAAAACAAAAAAACAGCCAAAACCCCCGTTTTTACCCCCCCCTTGGATTTTCAAACC
CTTTTTAAAATTTTTGAAAAAAAACCCCCAAACAAAATTAAATTTTTTCCCCCAAAAAAT
TTTTTTTTTTAACAAAAGGGGGGGTGGAAAATTTTTTTTTTCCCCCCCCCAAAAGGGGTT
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CACAAGGNAGTGGACGAGATGAGTGCGGGATCATCCCGCAGGCCATCCCAGGATCGGGGA
GGGAGGCCGGCCCCGCTGCAGAAAGGGGCTTCTGGGAGACCCCCCAGCCCAAGGCAGGAG
CCCGGGCGATTCCCGGGAGGCCGCAGGCGCTGGGCGAAGCGCTGGGCGAAGGGCCGCTGC
CAGCCGGGAGAGAATTCATAGGTTTGTTGAGGAGCAGAGGCCTGGGAACAAATTCGGGCG
GGCACGGCGGCTAGAACTGATCGCTACCAATTCGAGGAAGCCAGCAAGGCAGGTTCCGAG
GCCGCCTGCCCACCCGCAGCTTCTTGGACACTGCGCAAACCCTGCTGCGGCCAGGCTGGA
GCCTCCGATCACCAAACCAACACTCCCTGGCCTTCTGTTTCTTGATTCCTTAATTTTGAG
ATAAGACCGTCCCTAGCAGTGAGGCCTCGGCCTCTGTTCATTTAACTTCTCAAACCAAAC
TAGCCCTAATTCAGTTCACCCCAGAGCATCACCTGGTTTTATTTTTATTTTTTTATTTTT
TTATTTATTTTTTTTTTTTTTGCAGCCTGAAATTTTAAGTCACCGTTTGTCTCCCTCACC
AGGGTGTGAACTGCCCCGAGGGCAGAGACCTCCCGTTTTGTTTTCCAGCGCCTTGAGCCA
GCTTGACTTTTTACAAATGCTGAGTGAGACGTGTCGGTGGCTCCCAGTGCACTTGGCAGA
GTGAGCCGCAGCCAGCTGGGCGCTCCAGGCAGGACACAGTGGCCTCCACGAGGATCCCTT
ACCATTACTGTGCGGCCGCGCTCCGTAGGTCAAGCCGCTCTTACCAAGCGTCTTTCTGCC
TTTCTGTTCCCCCTCAGAGCTGTGCGCGCTGCAGAAGGCGGTGGAGCTGGAGAAGACAGA
GGCGGACAACGCGGAGCGGCCCCGGGCGCGACGGCGGAGGAAGCCGCGCGTGCTCTTCTC
GCAGGCGCAGGTCTATGAGCTGGAGCGGCGCTTCAAGCAGCAGCGGTACCTGTCGGCCCC
CGAACGCGACCAGCTGGCCAGCGTGCTGAAACTCACGTCCACGCAGGTCAAGATCTGGTT
CCAGAACCGGCGCTACAAGTGCAAGCGGCAGCGGCAGGACCAGACTCTGGAGCTGGTGGG
GCTGCCCCCGCCGCCGCCGCCGCCTGCCCGCAGGATCGCGGTGCCAGTGCTGGTGCGCGA
TGGCAAGCCATGCCTAGGGGACTCGGCGCCCTACGCGCCTGCCTACGGCGTGGGCCTCAA
TCCCTACGGTTATAACGCCTACCCCGCCTATCCGGGTTACGGCGGCGCGGCCTGCAGCCC
TGGCTACAGCTGCACTGCCGCTTACCCCGCCGGGCCTTCCCCAGCGCAGCCGGCCACTGC
CGCCGCCAACAACAACTTCGTGAACTTCGGCGTCGGGGACTTGAATGCGGTTCAGAGCCC

Fig. 4B 2

CGGGATTCCGCAGAGCAACTCGGGAGTGTCCACGCTGCATGGTATCCGAGCCTGGTAGGG
AAGGGACCCGCGTGGCGCGACCCTGACCGATCCCACCTCAACAGCTCCCTGACTCTCGTG
GGGAGAAGGGGCTCCCAACATGACCCTGAGTCCCCTGGATTTTGCATTCACTCCTGCGGA
GACCTAGGAACTTTTTCTGTCCCACGCGCGTTTGTTCTTGCGCACGGGAGAGTTTGTGGC
GGCGATTATGCAGCGTGCAATGAGTGATCCTGCAGCCTGGTGTCTTAGCTGTCCCCCCAG
GAGTGCCCTCCGAGAGTCCATGGGCACCCCCGGTTGGAACTGGGACTGAGCTCGGGCACG
CAGGGCCTGAGATCTGGCCGCCCATTCCGCGAGCCAGGGCCGGGCGCCCGGGCCTTTGCT
ATCTCGCCGTCGCCCGCCCACGCACCCACCCGTATTTATGTTTTTACCTATTGCTGTAAG
AAATGACGATCCCCTTCCCATTAAAGAGAGTGCGTTGACCCCGCACGTGTGCTTCTTTCA
GCTTGCGGCGCTTCAGAAGCAGGAGAGAGGTGGCCGCCCGGGACTGGTCTCAGATCTCAG
GCACAGGCATTCCCTGAGCAAATTGATAACATTGATACTAATAAAACCTAACCCTTGCTG
GAACCATACTGGTTCCGTGTCGGGCACTTTCTGAGATTGTCTCATATAATCCTCAATAAT
CCAAAAAAAAAAAAATCCTAAAGTTTAGAAGCTGAGGCCCGGAGAGGTTTAATGACTTAC
CTGCGAGCAAATAGCCAGTACTAGTCGAACTCTGGTTAAATTCAGGATGCCTCACTTCAG
AGACCGCCTTCCCTGTGCTCCCAAGCTCCCCTCCTTGAATCCTAATGTGTGCCAGGCACG
GTTCCAGGCACTGGGCATTAAATGGACAAGCAAAAGAACCTGGGCCCTCTGTAGCTGGAG
AGCACCGTGATCATCCCACTTAAAAGAACTCCTTAACCTGTTTCCAAGATGGNAAAAGCC
AAGAANCCAAAGCCCTTGGGNAAGCGTTCTCAAGGGTCCTCANATGCCCCAAATGCCACG
TCGGGGGCTCAACANCTNGCCCGTTGGAACTGAATGCCNANGGTGGGCCCCAAANAAGGN
TCCTGCGGGATGGNGCTCAACTCCAAGCTGTGGTGAAGGCCCATAAAATTCAAATGGGCC
AAGGGGAGCCCCCTAAAGCCCTAAACCTTCNGGGGGTCCNTTCCCTAAGGGCATTTAANT
TTACCAAAAGTTTGGNCAAANAATGTTTCCAATGGNCCNGATTTTATNGANGGGNAAAAC
TGGNGGGCAACCGAAATCCAGTTTAAACCCGGGTTGTTT (SEQ ID NO.: 5)

Fig. 4B 3

AGGCCCCCCG CACCCTCATC CTGGCTCCCG CCCCTTCTCT CCACCCTCCC
GGACCCCTAA AGGGGCGGCG GGGCCCAAGC CGAGGGCGCT GCGCCTGACC
CCGAGCGGAA GGGCCCCAGT CTAGGTCCTA ATGCGGGTGG CGTCTCCTTT
GACAGGCGGC GTTTGGGGAC AACAGCGGGG ACGAGAGATA AGGTGACATA
CCAGAGCAGA TTTGGTGCGC GCGCTGATAC TCCTCTCCCG ACAGGAAACG
CGGAGCTATT TAAAAGACCC TATCGATTAC TTTATCTTTC CTGGAAAGCT
TCTTGCGGAG AGACAAAAGA TGTTCCCTGC CTAAAGACAC AAGGCCACAC
AACGGAGGGT CTGCACAGGC GACGC (SEQ ID NO.: 1)

TGCTCCTTT TAAGGGCTTG AATGTCTGCA ACTGTCATGT GTACACTTAA
AG (SEQ ID NO.: 2)

Fig. 5A

AGGCCCCCCG CACCCTCATC CTGGCTCCCG CCCCTTCTCT CCACCCTCCC
GGACCCCTAA AGGGGCGGCG GGGCCCAAGC CGAGGGCGCT GCGCCTGACC
CCGAGCGGAA GGGCCCCAGT CTAGGTCCTA ATGCGGGTGG CGTCTCCTTT
GACAGGCGGC GTTTGGGGAC AACAGCGGGG ACGAGAGATA AGGTGACATA
CCAGAGCAGA TTTGGTGCGC GCGCTGATAC TCCTCTCCCG ACAGGAAACG
CGGAGCTATT TAAAAGACCC TATCGATTAC TTTATCTTTC CTGGAAAGCT
TCTTGCGGAG AGACAAAAGA TGTTCCCTGC CTAAAGACAC AAGGCCACAC
AACGGAGGGT CTGCACAGGC GACGCACAAT TCGGCGCGGG GAAAGCAAAA
ACACACTGAC GCTTAGAGTG CACAAACGTG TGTGTTCCCA GAGCAGCTCC
AGAGTGCGGC AGGGACGCTG GGGGCGGCGA GGGGCACCCA CAGTATGGTC
TTCTGTGCCC TTGGAAAGTT TTTTTTCACC GTATGCGCGT AAAACACGCA
CACACAGAGA AAGTGACTGT GCACTTAGGG CGCCTGTGTG TACCCGTGTC
GTTTTAGCGA ATTTAAAGCA CATCAGGCCG GGCGCCATGG CTCACGCCTG
TAATCCCAGC ACTTTAGGAG GCCGAGGCGG GCCGATCACC TGAGGTCGGG
AGTTCGACAC CAGCCTGGCC AACATGGTGA AACCCTGTCT CTACAAAAAA
TACAAAAAAT AGCCGGGCAT GGTGATGCGT GCCTGTGATC CCAGCTACTC
GGGAGGCTGA GGCAGGAGAA TCGCTTGAAC CCGGGAGGCG GAGGTTGCAG
TGAGCCGAGA TCACACCACT GCACTCCAGC CTGGGCGACA AGAGCGAAAT
TCCGTCTAAA AAAATAAAAT AAAATAAAAT GATAATTAAG CCCATCAACT
CACATTCAAA GCGGTTACTG GTGGTTGTAA TGTATCCATA GACACAGGTC
TAAAATGTAA ACGCTCCATT GTGCTCCTTT TAAGGGCTTG AATGTCTGCA
ACTGTCATGT GTACACTTAA AG (SEQ ID NO.: 3)

Fig. 5B

AGAGAAATCA TTACCCGATT CACAAAGAGC ATAGAGAGTG TAACAGTCAC
TGATCTTGTT CAAATAGGGA GAGTTTTTTT TCCTTCCCTT TTTGTAACAC
CTGACCCACA GGACTGACAG TTCTAGGAAG CCCCCTTACC CGAAAATAGG
AAATAAATCC TTGCCACCTT GATTTGCAAG GGCAATGCTA ATTTTTTTCT
TTCTCCAGAG CTCTCAAAAA AAAAAAAAAA AAAACCTTAC TAAAAACAGG
GATCCCGGAT GTAGCCTCGA TGTCCCCCAT TAAACGGTAA TATTTCAGGC
GTCCGCTCAC ACTAATCTTT CAAACTGTCA TCGCGAGCCG CCTGGCCAGC
AGATTCACTT AACAGCGCTC CCAGGACCCT CGTTCCGAGC TCTTTTCAGC
GAGACATTTA ATTGAATCGG ATGTGGCTCG TTTGCCAGAC GTCACCGCCT
CGGCGATAGG CATCCTCTCC AACGACAC (SEQ ID NO.: 6)

Fig. 5C

Transgenic Constructs of the Human Csx/Nkx2-5 Enhancer

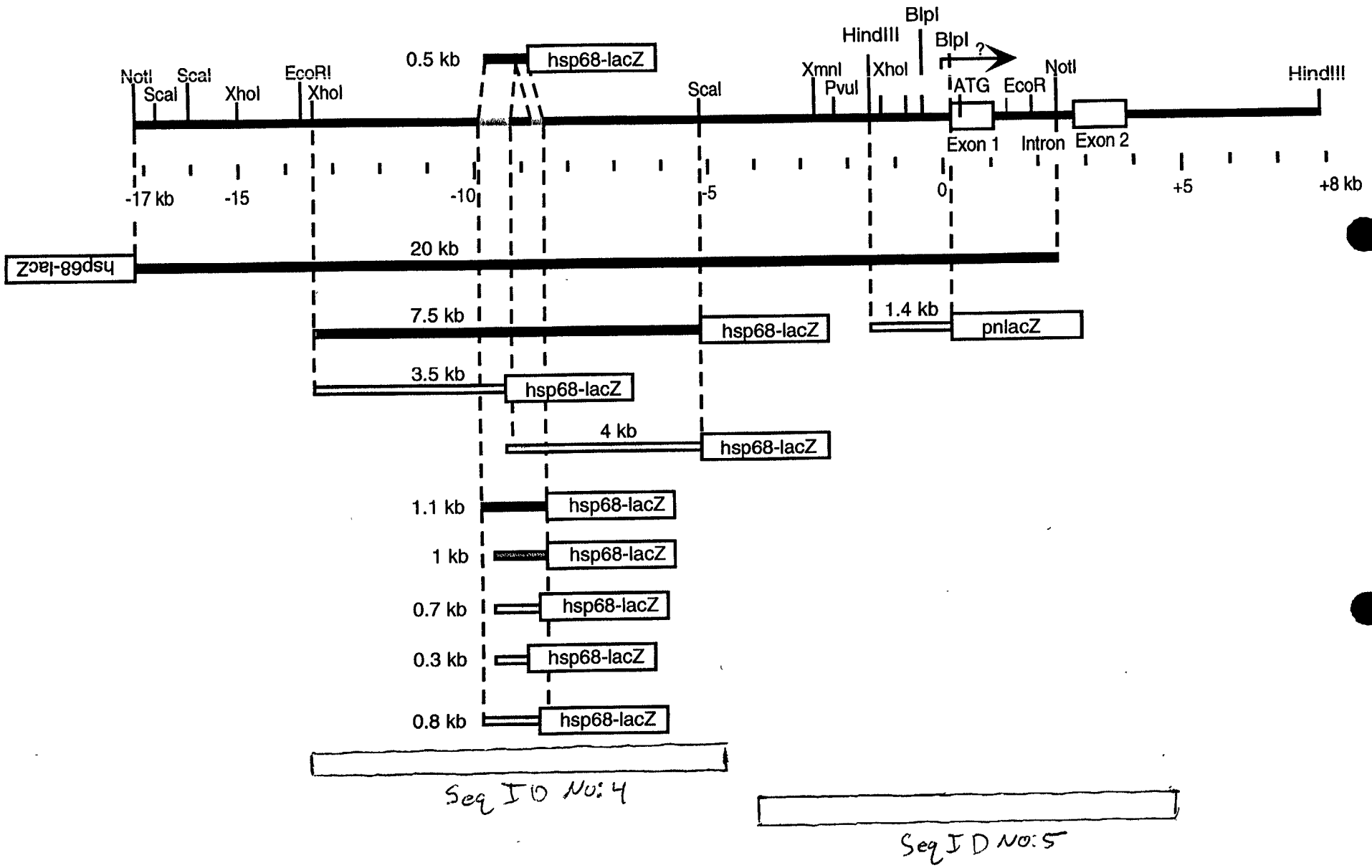


Fig. 6

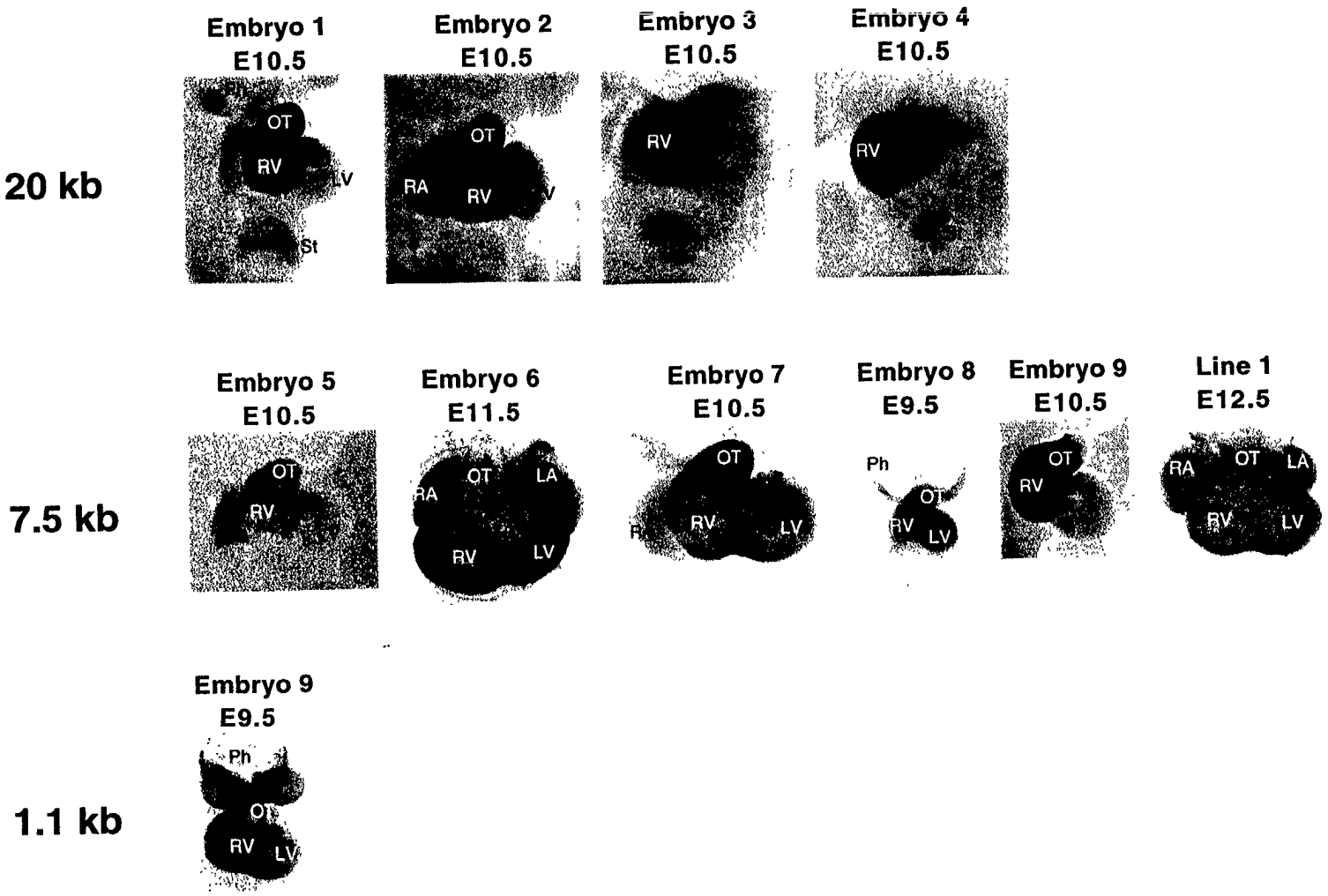
Transgenic Analysis of the Human Csx Enhancer Sequence

Constructs	# of Transgenes	Enhancer positives (Cardiac : Ectopic)[1]
20 kb	8	4 : 0
7.5 kb	8	6 : 1
promoter-proximal 4 kb	7	0 : 1
promoter-distal 3.5 kb	6	0 : 0
1.1 kb	8	3 : 1
1.0 kb	10	1 : 2
0.7 kb	8	0 : 3
0.3 kb	11	0 : 6
0.8 kb	6	0 : 1
0.5 kb	2	2 : 0

1. Each embryo was classified into either 'cardiac' or 'ectopic' judged upon the extent of similarity to the endogenous Csx expression pattern.

Fig. 7

Cardiac Expression of the hCsx Enhancer-hsp68-lacZ Constructs

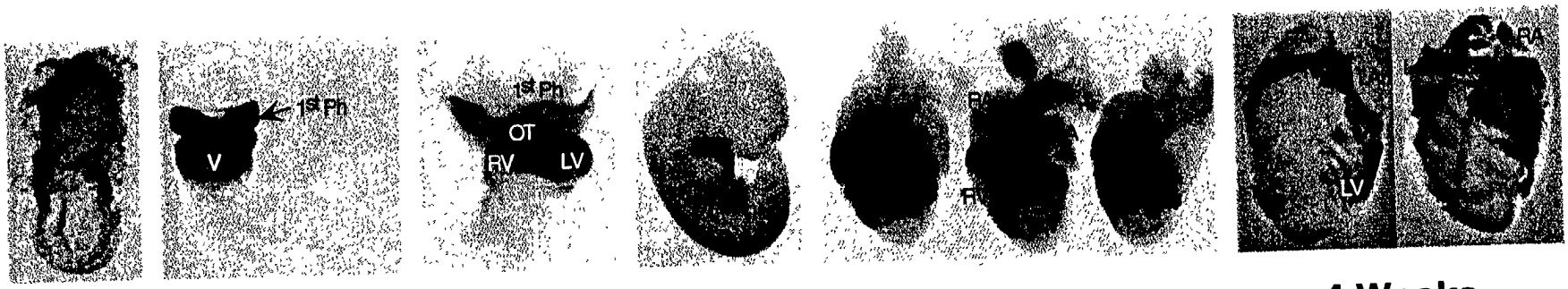


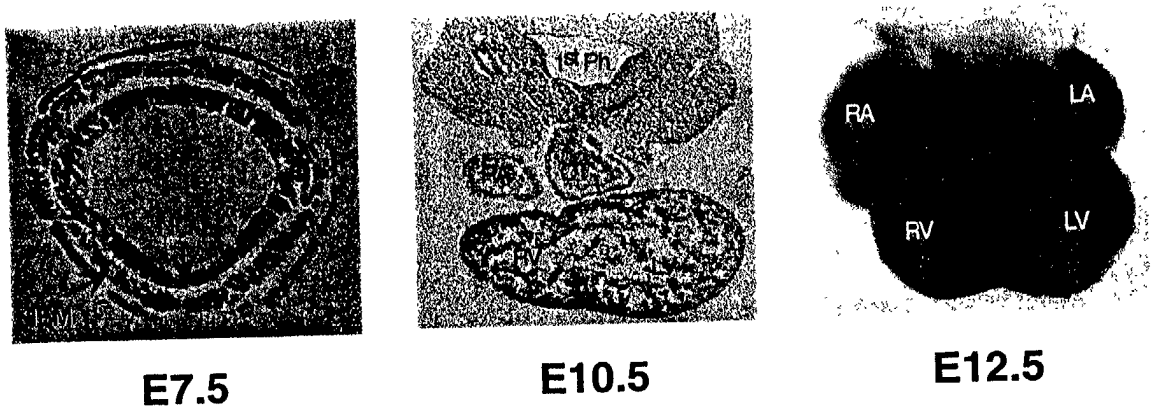
RA; Right Atrium LA; Left Atrium RV; Right Ventricle LV; Left Ventricle

Ph; Pharyngeal Arch St; Stomach OT; Outflow Tract

Fig. 8

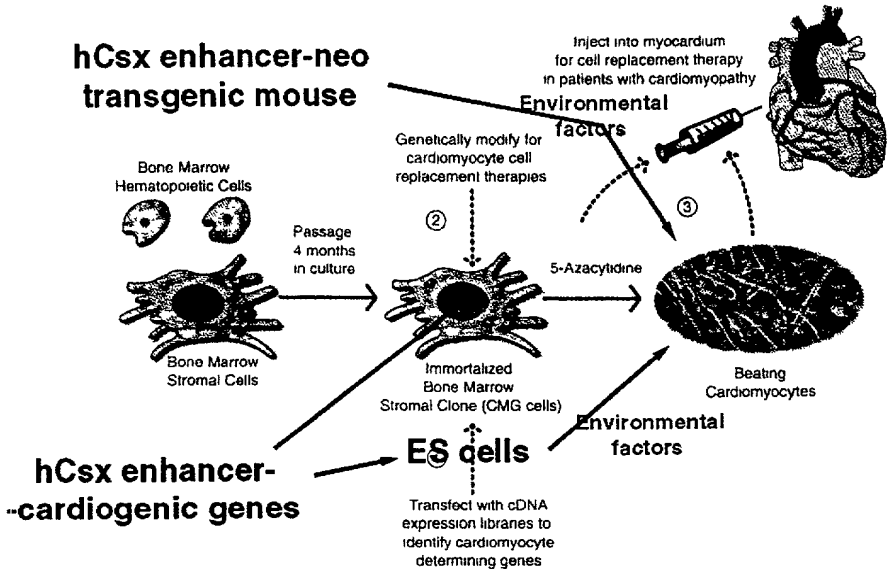
Cardiac Expression of the 7.5 kb hCsx Enhancer-hsp68-lacZ Construct





RA; Right Atrium LA; Left Atrium
RV; Right Ventricle LV; Left Ventricle
OT; Outflow Tract Ph; Pharyngeal Arch
IEM; Intra Embryonic Mesoderm
NG; Neural Groove

Fig. 9



Facilitated isolation of cardiac myocytes.
Modified from [J. M. Leiden, JCI (1999) 103:591]

Fig. 10